

**CLAIMS**

What is claimed is:

1. A method for directly identifying a non-endogenous compound as a compound  
5 having an activity selected from the group consisting of: inverse agonists, parallel  
agonists, and partial agonists, to a non-endogenous, constitutively activated version  
of known G protein-coupled receptor, said receptor comprising a transmembrane-6  
region and an intracellular region, comprising the steps of:  
10 (a) selecting a non-endogenous version of a known GPCR having an amino  
acid sequence selected from the group consisting of SEQ.ID.NO.:425;  
SEQ.ID.NO.:427; SEQ.ID.NO.:429; SEQ.ID.NO.:431;  
SEQ.ID.NO.:433; SEQ.ID.NO.:435; SEQ.ID.NO.:437;  
SEQ.ID.NO.:439; SEQ.ID.NO.:441; SEQ.ID.NO.:443;  
SEQ.ID.NO.:445; SEQ.ID.NO.:447; SEQ.ID.NO.:449;  
15 SEQ.ID.NO.:451; SEQ.ID.NO.:453; SEQ.ID.NO.:455;  
SEQ.ID.NO.:457; SEQ.ID.NO.:459; SEQ.ID.NO.:461;  
SEQ.ID.NO.:463; SEQ.ID.NO.:465; SEQ.ID.NO.:467;  
SEQ.ID.NO.:469; SEQ.ID.NO.:471; SEQ.ID.NO.:473;  
SEQ.ID.NO.:475; SEQ.ID.NO.:477; SEQ.ID.NO.:479;  
20 SEQ.ID.NO.:481; SEQ.ID.NO.:483; SEQ.ID.NO.:485;  
SEQ.ID.NO.:487; SEQ.ID.NO.:489; SEQ.ID.NO.:491;  
SEQ.ID.NO.:493; SEQ.ID.NO.:495; SEQ.ID.NO.:497;  
SEQ.ID.NO.:499; SEQ.ID.NO.:501; SEQ.ID.NO.:503;  
SEQ.ID.NO.:505; SEQ.ID.NO.:507; SEQ.ID.NO.:347;

SEQ.ID.NO.:509; SEQ.ID.NO.:351; SEQ.ID.NO.:355;  
SEQ.ID.NO.:359; SEQ.ID.NO.:363; SEQ.ID.NO.:367;  
SEQ.ID.NO.:371; SEQ.ID.NO.:375; SEQ.ID.NO.:379;  
SEQ.ID.NO.:383; SEQ.ID.NO.:387; SEQ.ID.NO.:391;  
5 SEQ.ID.NO.:511; SEQ.ID.NO.:513; SEQ.ID.NO.:515;  
SEQ.ID.NO.:517; SEQ.ID.NO.:519; SEQ.ID.NO.:521;  
SEQ.ID.NO.:523; SEQ.ID.NO.:525; SEQ.ID.NO.:527;  
SEQ.ID.NO.:529; SEQ.ID.NO.:531; SEQ.ID.NO.:533;  
SEQ.ID.NO.:535; SEQ.ID.NO.:537; SEQ.ID.NO.:539;  
10 SEQ.ID.NO.:541; SEQ.ID.NO.:543; SEQ.ID.NO.:545;  
SEQ.ID.NO.:547; SEQ.ID.NO.:549; SEQ.ID.NO.:551;  
SEQ.ID.NO.:553; SEQ.ID.NO.:555; SEQ.ID.NO.:557;  
SEQ.ID.NO.:559; SEQ.ID.NO.:561; SEQ.ID.NO.:563;  
SEQ.ID.NO.:565; SEQ.ID.NO.:567; SEQ.ID.NO.:569;  
15 SEQ.ID.NO.:571; SEQ.ID.NO.:573; SEQ.ID.NO.:575;  
SEQ.ID.NO.:577; SEQ.ID.NO.:395; SEQ.ID.NO.:399;  
SEQ.ID.NO.:403; SEQ.ID.NO.:407; SEQ.ID.NO.:411;  
SEQ.ID.NO.:415; SEQ.ID.NO.:419; SEQ.ID.NO.:423;  
SEQ.ID.NO.:579; and SEQ.ID.NO.:581;

20 (b) confirming that the selected non-endogenous GPCR of step (a) is constitutively active;

(c) contacting a non-endogenous candidate compound with the non-endogenous, constitutively activated GPCR of step of (b); and

(d) determining, by measurement of the compound efficacy at said contacted receptor, whether said non-endogenous compound having inverse agonist activity as an inverse agonist or agonist activity is an agonist to said receptor of step (b).

5        2. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:425.

          3. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:427

          4. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:429.

10        5. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:431.

          6. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:433.

          7. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:435.

15        8. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:437.

          9. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:439.

20        10. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:441.

          11. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:443.

12. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:445.

13. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:447.

5 14. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:449.

15. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:451.

10 16. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:453.

17. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:455.

18. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:457.

15 19. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:459.

20. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:461.

21. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:463.

20 22. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:465.

23. The method of claim 1 wherein the non-endogenous GPCR of 467.

24. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:469.

25. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:471.

5 26. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:473.

27. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:475.

10 28. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:477.

29. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:479.

30. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:481.

15 31. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:483.

32. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:485.

33. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:487.

20 34. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:489.

35. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:491.

36. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:493.

37. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:495.

5 38. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:497.

39. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:499.

10 40. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:501.

41. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:503.

42. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:505.

15 43. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:507.

44. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:347.

45. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino 20 acid sequence having the sequence of SEQ.ID.NO.:509.

46. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:351.

47. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:355.

48. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:359.

49. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:361.

5 50. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:367.

51. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:371.

10 52. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:375.

53. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:379.

54. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:383.

15 55. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:387.

56. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:391.

57. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino 20 acid sequence having the sequence of SEQ.ID.NO.:511.

58. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:513.

59. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:515.

60. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:517.

61. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:519.

5 62. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:521.

63. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:523.

10 64. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:525.

65. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:527.

66. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:529.

15 67. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:531.

68. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:533.

69. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino 20 acid sequence having the sequence of SEQ.ID.NO.:535.

70. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:537.

71. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:539.

72. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:541.

73. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:543.

5 74. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:545.

75. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:547.

10 76. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:549.

77. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:551.

78. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:553.

15 79. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:555.

80. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:557.

81. The method of claim 1 wherein the non-endogenous GPCR of step b is step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:559.

20 82. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:561.

83. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:563.

84. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:565.

85. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:567.

5 86. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:569.

87. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:571.

10 88. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:573.

89. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:575.

90. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:577.

15 91. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:395.

92. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:399.

93. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:403.

20 94. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:407.

95. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:411.

96. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:415.

97. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:419.

5 98. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:423.

99. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:579.

10 100. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:581.

101. The method of claim 1 further comprising the following step:

15 *sub a* assessing, by using an endogenous ligand based assay, the impact of the non-endogenous compound of step (d) on the binding of an endogenous ligand for the known GPCR version of the non-endogenous version of said known GPCR of step (a) with said known GPCR.

3 102. The method of claim 101 wherein said non-endogenous compound is an allosteric modulator of said known GPCR.

*add  
a2*